REMARKS

The Office Action mailed December 31, 2002, has been received and reviewed. The Office Action identifies claims 1 and 26 through 36 as currently pending in the application. All claims stand rejected. Applicants have canceled claim 1, amended claims 26, 27, 28, 29, 30, 31, 32, 35 and 36 and added new claim 37. Applicants respectfully request reconsideration of the application as amended. Applicants gratefully note the removal of the rejection of claims 26, 27, 32 and 34 under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter, in view of the prior amendment and remarks, and the removal of the rejection of claims 1 and 26-36 under 35 U.S.C. § 102(a), in view of the 37 C.F.R. § 1.131 Affidavit. The remaining issues are addressed below.

Specification

The abstract of the disclosure was objected to in the Office Action with respect to the use of the word "said" therein. Applicants have amended the Abstract herein to remove this wording and respectfully submit that no further action should be required on this point.

Claim Objections

Claim 29 was objected to in the Office Action with respect to the wording "farm-animal." Applicants have amended the claim as suggested in the Office Action and respectfully submit that no further action is required on this point.

Claim 1 was objected to in the Office Action as assertedly reading on a non-elected invention. Applicants have canceled claim 1 herein, rendering this objection moot.

35 U.S.C. § 112, First Paragraph Rejections

Claims 1 and 26-36 were rejected in the Office Action as assertedly lacking enablement under 35 U.S.C. § 112, first paragraph. Claim 1 has been canceled, rendering this rejection moot as to it. Applicants respectfully submit that the remaining claims, as amended are enabled and request this rejection

be withdrawn and the claims allowed.

The Office Action states that the specification while

> "enabling for 1) A transgenic farm mammal, whose genome comprises a stably integrated recombinant nucleic acid encoding a polymeric immunoglobulin receptor (pIgR) protein, wherein said mammal over-expresses said pIgR protein in its mammary gland compared to the expression of the pIgR protein in a mammary gland of a wild-type farm mammal, and wherein said protein is capable of transporting a first immunoglobulin protein across the basolateral side of a mammary epithelial cell to the epithelial cell's apical side, wherein the first immunoglobulin is selected form the group consisting of IgM and IgA and the second protein is IgG; 2) A method of making the transgenic farm animal of 1, said method comprising: producing a DNA construct comprising a nucleic acid encoding pIgR protein operably linked to a promoter capable of driving expression of said pIgR protein in a mammary epithelial cell; introducing said DNA construct into fertilized eggs; and implanting the fertilized eggs into a pseudopreganant female farm mammal, thereby product the transgenic farm mammal of 1), whereby the concentration of IgM or IgA is increased on the mammary gland cell's apical side compared to IgG on the mammary gland's basolateral side; 3) A method of collecting an immunoglobulin protein selected from IgM or IgA from the transgenic farm mammal of 2), comprising: providing the transgenic farm mammal of 2; and collecting milk comprising said immunoglobulin protein from the mammary gland of said transgenic farm mammal" (Office Action at pages 3-4)

does not provide enablement for the claims. Applicants have amended the claims herein and respectfully submits that the amended claims are enabled and should be allowed.

The Office Action states that the claimed invention is "directed to making and using a transgenic animal" and the "state of the art teaches how to make and use transgenic mammals" (Office Action at page 4), and that "the claimed invention is only enabled for making and/or using transgenic non-human farm mammals" (Office Action at page 7, referring to claims 1. 26, 32, 33 and 34). Although Applicants respectfully disagree, independent claim 26 has been amended to be directed to a "transgenic mammalian farm animal" and the remaining claims have been similarly amended for consistency. Applicants thus respectfully submit that claim 26-36 are enabled and should be allowed.

Further, the Office Action states that the "claims read on a transgenic farm animal whose genome comprises a recombinant nucleic acid encoding pIgR protein, wherein the protein has a function limitation and does not recite a phenotype." This statement is followed by a note that "the broadest interpretation

of the claimed non-human farm animal having cells, which harbor a recombinant nucleic acid that expresses the protein at a level sufficient to result in a specific phenotype" (Office Action at page 5). The Office Action thus notes that the broadest reasonable interpretation of the claims assigned by the Examiner include a specific phenotype. Accordingly, Applicants request this rejection be withdrawn on this ground, and the claims allowed.

Further, as amended, Applicants respectfully submit that the inclusion of a level of over-expression of pIgR in the claims, as suggested by the Office Action be reconsidered. At the paragraph spanning pages 14-15 of the application as-filed, a level of pIgR expression is detected in transgenic mammals. Such levels are correlated with the level of immunoglobulin detected in the milk of several transgenic mammals in Table 1, on page 28 of the application as filed. This description clearly shows a dose dependency, the higher the level of pIgR, the higher the antibody content of the milk. The set -up was not designed to measure small differences, such as the those at the extreme lower end of the expression continuum. However, this does not mean that such differences were not present. No mechanism can be envisioned where such differences would not be present. Any level of over-expression will inevitably lead to an increase in the amount of the first class immunoglobulin in the milk. It is respectfully submitted that claim 26, as amended is supported by the application as filed, and such an requirement is not necessary. Applicants respectfully request claim 26, with the claims dependent therefrom be allowed.

With respect to the rejection of claim 31 on page 8 of the Office Action, the Office Action states that "the as-filed specification fails to provide sufficient guidance of evidence for how one skilled in the art would be enabled for using a casein promoter in any cell other than epithelial cells in a mammary gland." Accordingly, Applicants have amended claim 31 and it is respectfully submitted that amended claim 31 is enabled. It is requested that amended claim 31 be allowed.

Claims 26, 29, 30, 31, 32, 33, 35 and 36 were rejected as assertedly lacking enabled on pages 8 and 9 of the Office Action, with reference to the language of "transporting an immunoglobulin protein from the cell's basolateral side to a the cell's apical side. The Office Action cites Lamm, G614 for the proposition that: "Immunoglobulins that are not polymeric, such as IgG, have no physiological means of

reaching external secretions." (Office Action at page 8). Accordingly, Applicants have amended claim 26 to read "said protein is capable of transporting a polymeric immunoglobulin protein across the basolateral side of an epithelial cell's apical side, resulting in over-expression of the polymeric immunoglobulin protein on the epithelial cell's apical side" and the remaining claims amended accordingly. It is respectfully submitted that amended claims 26, 29, 30, 31, 32, 33, 35 and 36 are enabled and it is requested they be allowed.

With respect to claim 32, the Office Action states that "the specification only teaches how to collect milk from a transgenic mammal that over-expresses pIgR in the mammary gland and does not teach how to collect milk from a transgenic farm mammal that does not over-express pIgR in its mammary gland." As amended, claim 32 includes: "collecting milk comprising said polymeric immunoglobulin protein from the mammary gland of said transgenic mammalian farm animal." In order for the polymeric immunoglobulin protein to be present in sufficient quantities in the milk, such over-expression must occur in a mammary gland epithelial cell. Accordingly, Applicants respectfully submit that claim 32 is enabled. Further, Applicants respectfully submit that collecting milk from any mammalian farm animal is well-known in the art. Accordingly, it is requested that amended claim 32 be allowed.

Claim 35 was rejected in the Office Action as assertedly lacking enablement. The Office Action states that the breadth "of the claim reads on using the proteins with any promoter (endogenous or exogenous) to enhance expression of pIgR in transgenic farm mammal." Applicants initially note that amended claim 35 reads:

> 35. The method according to claim 31, comprising administering a protein capable of enhancing the expression of pIgR in the transgenic mammalian farm animal prior to collecting milk from the mammary gland, the protein selected from the group consisting of interferon-γ, interleukin-1, interleukin-4, and tumor necrosis factor-χ.

A promoter is thus not an element of this claim. At page 9, lines 12-19 of the as-filed application, expression of the nucleic acid encoding a protein and use of a promoter is discussed. In view of this discussion, and the claim language, Applicants respectfully submit that claim 35 is enabled and requests it be allowed.

35 U.S.C. § 112, Second Paragraph Rejections

Claims 27, 32 and 36 were rejected in the Office Action under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants respectfully submit that, as amended, these claims are definite and request they be allowed.

Claim 27 was rejected as assertedly indefinite with respect to the term "immunoglobulin protein." The Office Action states that claim 27, depending from claim 26, does not define which protein is being claimed. Applicants have amended claims 26 and 27 to clearly identify the "polymeric immunoglobulin protein" forming an element of those claims. It is respectfully submitted that amended claim 27 is definite, and Applicants request it be allowed.

Claim 32 was rejected in the Office Action as assertedly indefinite with respect to the language "an animal" in the claim. Claim 32 has been amended along the lines suggested in the Office Action, and now recites: "the transgenic mammalian farm animal from claim 26". It is respectfully submitted no further action is required on this point and requested the claim be allowed.

Claim 36 was rejected as assertedly indefinite as lacking antecedent basis with respect to the language "administering an antigen to said farm animal prior to collecting the milk from the mammary gland". Applicants have amended claim 31 to provide proper antecedent basis. It is respectfully submitted that claim 36 is definite and Applicants request it be allowed.

CONCLUSION

All claims are believed to be in condition for allowance, and an early notice thereof is respectfully solicited. Should the Office determine that additional issues remain which might be resolved by a telephone conference, the Examiner is respectfully invited to contact Applicants' undersigned attorney.

Respectfully submitted,

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Date: October 17, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please replace the Abstract appearing on page 38 of the application with the following replacement Abstract:

Abstract

Methods and processes for raising the concentration of a first class of immunoglobulin relative to at least a second class of immunoglobulin in a compartment of the body of a non-human animal or the progeny thereof, as well as the animals produced by such methods and processes. Such methods and processes provide for the collection of antibodies produced by mucosal surfaces of the animal. Preferably, the production is in the mammary gland. Antibodies can be collected from the milk of [said] the animal. Antibodies may be used for medical and/or nutritional purposes.

IN THE CLAIMS:

Please amend the claims as follows:

26. (Amended) A transgenic mammalian farm animal having a genome, the genome comprising a recombinant nucleic acid encoding a polymeric immunoglobulin receptor (pIgR) protein, wherein said protein is capable of transporting [an] a polymeric immunoglobulin protein across the basolateral side of an epithelial cell's apical side, resulting in over-expression of the polymeric immunoglobulin protein on the epithelial cell's apical side in comparison to another immunoglobulin protein located on the epithelial cell's basolateral side.

27. (Twice Amended) The transgenic mammalian farm animal of claim 26, wherein the polymeric immunoglobulin protein is selected from the group consisting of IgM and IgA.

28. (Amended) The transgenic mammalian farm animal of claim 26, wherein the immunoglobulin protein located on the epithelial cell's basolateral side is IgG.

29. (Amended) The transgenic mammalian farm animal of claim 26, wherein said transgenic mammalian farm animal over-expresses said pIgR protein at least 10-fold higher than the expression of the pIgR protein in the wild-type of said mammalian farm [-] animal.

30. (Amended) A method of making the transgenic mammalian farm animal of claim 26, said method comprising:

producing a DNA construct comprising a nucleic acid encoding a pIgR protein operably linked to a promoter capable of driving expression of said pIgR protein in [an] a mammary gland epithelial cell;

introducing said DNA construct into fertilized eggs; and

implanting the fertilized eggs comprising said DNA construct into a pseudopregnant female mammalian farm

animal, thereby producing the transgenic mammalian farm animal according to claim 26.

31. (Amended) The method according to claim 30, wherein said promoter capable of driving expression of said pIgR protein in [an] a mammary gland epithelial cell is a casein promoter.

32. (Amended) A method of collecting an immunoglobulin from the transgenic mammalian farm animal of claim 26, comprising:

providing [a] the transgenic mammalian farm animal from claim 26, whose genome comprises a recombinant nucleic acid encoding a polymeric immunoglobulin receptor (pIgR) protein, which said protein is capable of transporting [an] a polymeric immunoglobulin protein across the basolateral side of an epithelial cell to the epithelial cell's apical side, resulting in over-expression of the polymeric immunoglobulin protein on the epithelial cell's apical side compared to another immunoglobulin protein located on the epithelial cell's basolateral side; and

collecting milk comprising said polymeric immunoglobulin protein from the mammary gland of said transgenic mammalian farm animal.

35. (Amended) The method according to claim 31, comprising administering a protein capable of enhancing the expression of pIgR in the transgenic mammalian farm animal prior to collecting milk from the mammary gland, the protein selected from the group consisting of interferon-γ, interleukin-1, interleukin-4, and tumor necrosis factor-χ.

36. (Amended) The method according to claim 31, comprising administering an antigen to said transgenic mammalian farm animal prior to collecting the milk from the mammary gland